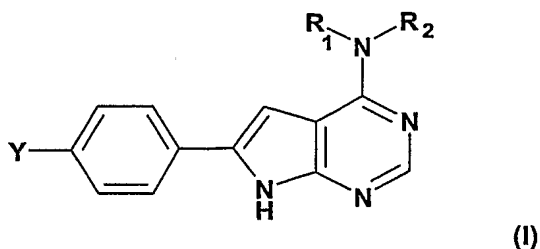


Claims

1. A compound of formula I,



wherein

R_1 and R_2 are independently hydrogen, halo; or lower alkyl, heterocycle, amino or cycloalkyl all of which may be unsubstituted or substituted;

or R_1 and R_2 can join together to form an unsubstituted or substituted N-heterocycle;

Y is $(R_3)_n-X-$ or $A(R_3)(R_3)C-$

wherein

X is lower alkyl, amino, amido or carbonyl;

A is hydroxy, amino, halo, or lower alkyl;

R_3 is lower alkyl, lower alkoxy, carbonyl, amino, hydroxy, heterocycle or heteroaryl all of which can be unsubstituted or substituted;

n is 1 or 2;

the substituents on R_3 are one or more substituents independently selected from the group consisting of halo, lower alkyl, lower alkoxy, amino, hydroxy and heterocycle; all of which, except halo, are unsubstituted or substituted by one or more substituents independently selected from the group consisting of halo, hydroxy, lower alkoxy, amino, lower alkyl and heterocycle; all of which, except halo, are unsubstituted or substituted by one or more substituents independently selected from the group consisting of halo, lower alkyl, lower alkoxy, hydroxy and lower alkoxy;

the substituents on R_1 and R_2 are one or more substituents independently selected from the group consisting of halo, hydroxy, lower alkyl, lower alkoxy, amino, cycloalkyl, heterocycle and heteroaryl; all of which, except halo, are unsubstituted or substituted by one or more substituents independently selected from the group consisting of halo, hydroxy, lower alkyl, lower alkoxy, amino, heterocycle and heteroaryl; all of which, except halo, are unsubstituted or substituted by one or more substituents independently selected from the group consisting of halo, hydroxy, loweralkyl and amino;

or a pharmaceutically acceptable salt, ester thereof.

2. A compound of formula I according to claim 1,

wherein

R_1 and R_2 are independently hydrogen, halo; or lower alkyl, heterocycle selected from pyrrolidine, tetrahydrothiophene, tetrahydrofuran, piperidine, pyran, pyrazolidine, oxirane, dioxane, imidazoline, imidazolidine, morpholino and piperazine, amino or cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl; all of which may be unsubstituted or substituted;

or R_1 and R_2 can join together to form an unsubstituted or substituted N-heterocycle selected from pyrrolidine, imidazoline, imidazolidine, piperidine, morpholino, and piperazine;

Y is $(R_3)_n-X-$ or $A(R_3)(R_3)C-$;

wherein

X is lower alkyl, amino, amido or carbonyl;

A is hydroxy, amino, halo, or lower alkyl;

R_3 is lower alkyl, lower alkoxy, carbonyl, amino, hydroxy, heterocycle selected from pyrrolidine, tetrahydrothiophene, tetrahydrofuran, piperidine, pyran, pyrazolidine, oxirane, dioxane, imidazoline, imidazolidine, morpholino and piperazine, or heteroaryl selected from pyridyl, indoyl, quinoxaliny, quinoliny, isoquinoliny, benzothienyl, benzofuranyl, benzopyranyl, benzothiopyranyl, furanyl, pyrrolyl, thiazolyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl, pyrazolyl, imidazolyl and thienyl, all of which may be unsubstituted or substituted; n is 1 or 2;

the substituents on R_3 are one or more substituents independently selected from the group consisting of halo, lower alkyl, lower alkoxy, amino, hydroxy and heterocycle selected from pyrrolidine, tetrahydrothiophene, tetrahydrofuran, piperidine, pyran, pyrazolidine, oxirane, dioxane, imidazoline, imidazolidine, morpholino and piperazine; all of which, except halo, are unsubstituted or substituted by one or more substituents independently selected from the group consisting of halo, hydroxy, lower alkoxy, amino, lower alkyl and heterocycle selected from pyrrolidine, tetrahydrothiophene, tetrahydrofuran, piperidine, pyran, pyrazolidine, oxirane, dioxane, imidazoline, imidazolidine, morpholino and piperazine; all of which, except halo, are unsubstituted or substituted by one or more substituents independently selected from the group consisting of halo, lower alkyl, lower alkoxy, hydroxy and lower alkoxy; the substituents on R_1 and R_2 are one or more substituents independently selected from the group consisting of halo, hydroxy, lower alkyl, lower alkoxy, amino, cycloalkyl selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl, heterocycle selected from pyrrolidine, tetrahydrothiophene, tetrahydrofuran, piperidine, pyran,

pyrazolidine, oxirane, dioxane, imidazoline, imidazolidine, morpholino and piperazine and heteroaryl selected from pyridyl, indoyl, quinoxaliny, quinoliny, isoquinoliny, benzothienyl, benzofuranyl, benzopyranyl, benzothiopyranyl, furanyl, pyrrolyl, thiazolyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl, pyrazolyl, imidazolyl and thienyl, all of which, except halo, are unsubstituted or substituted by one or more substituents independently selected from the group consisting of halo, hydroxy, lower alkyl, lower alkoxy, amino, heterocycle selected from pyrrolidine, tetrahydrothiophene, tetrahydrofuran, piperidine, pyran, pyrazolidine, oxirane, dioxane, imidazoline, imidazolidine, morpholino and piperazine and heteroaryl selected from pyridyl, indoyl, quinoxaliny, quinoliny, isoquinoliny, benzothienyl, benzofuranyl, benzopyranyl, benzothiopyranyl, furanyl, pyrrolyl, thiazolyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl, pyrazolyl, imidazolyl and thienyl,; all of which, except halo, are unsubstituted or substituted by one or more substituents independently selected from the group consisting of halo, hydroxy, loweralkyl and amino; or a pharmaceutically acceptable salt, ester thereof.

3. A compound of formula I according to claim 1, wherein

R_1 and R_2 are independently hydrogen, lower alkyl, cycloalkyl, hydroxy-lower alkyl, lower alkoxy-lower alkyl, lower alkyl-amino-lower alkyl, heterocycle-lower alkyl;

or R_1 and R_2 can join together to form a N-heterocycle or lower alkyl-N-heterocycle;

Y is $(R_3)_n$ -X- or $A(R_3)(R_3)C$ -;

wherein

X is lower alkyl or carbonyl;

A is hydroxy;

n is 1;

R_3 is lower alkyl, lower alkoxy, amino, heterocycle, heteroaryl, lower alkyl-heterocycle, heterocycle-lower alkyl, lower alkyl-amino-lower alkyl, heterocycle-lower alkyl-amino, lower alkyl-amino, hydroxy-lower alkyl-amino, amino substituted by lower alkoxy-lower alkyl and lower alkyl;

or a pharmaceutically acceptable salt or ester thereof;

heterocycle is selected from pyrrolidine, tetrahydrothiophene, tetrahydrofuran, piperidine, pyran, pyrazolidine, oxirane, dioxane, imidazoline, imidazolidine, morpholino and piperazine; cycloalkyl is selected from cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl, cycloheptyl and cyclooctyl;

N-heterocycle is selected from pyrrolidine, imidazoline, imidazolidine, piperidine, morpholino, and piperazine;

heteroaryl is selected from pyridyl, indoyl, quinoxaliny, quinoliny, isoquinoliny, benzothienyl, benzofuranyl, benzopyranyl, benzothiopyranyl, furanyl, pyrrolyl, thiazolyl, oxazolyl, isoxazolyl, triazolyl, tetrazolyl, pyrazolyl, imidazolyl and thienyl.

4. A compound of formula I according to claim 1, 2 or 3,

R₁ and R₂ are independently hydrogen, methyl, ethyl, propyl, cyclopropyl, hydroxy-propyl, dimethylamino-ethyl, morpholinyl-propyl, methoxy-ethyl, pyrrolidinyl-propyl;

or R₁ and R₂ can join together to form a piperazinyl or methyl-piperazinyl, preferably N-methyl-piperazinyl;

Y is (R₃)_n-X- or A(R₃)(R₃)C-;

wherein

X is CH₂ or -C(O)-;

A is hydroxy;

n is 1;

R₃ is methyl, ethyl, butoxy, morpholinyl, piperazinyl, pyrrolyl, tetrazoyl, imidazoyl, methyl-piperazinyl, diethyl-amino-propyl, morpholino-propyl-amino, methyl-amino, hydroxy-propyl-amino, (methoxy-ethyl)methyl-amino;

or a pharmaceutically acceptable salt or ester thereof.

5. A compound of formula I according to claim 1, 2, 3 or 4, selected from the group consisting of

methyl-{6-[4-(4-methyl-piperazin-1-ylmethyl)phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}-propylamine;

[4-(4-methylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phenyl]-morpholin-4-yl-methanone;

[4-(4-dimethylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phenyl]-(4-methyl-piperazin-1-yl)-methanone;

dimethyl-{6-[4-(4-methyl-piperazin-1-ylmethyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}-amine;

N-(3-diethylamino-propyl)-4-(4-dimethylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-benzamide;

[4-(4-dimethylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phenyl]-morpholin-4-yl-methanone;

4-(4-dimethylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-N-(3-morpholin-4-yl-propyl)-benzamide;

(4-methyl-piperazin-1-yl)-{4-[4-(4-methyl-piperazin-1-yl)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-phenyl}-methanone;

4-(4-methyl-piperazin-1-yl)-6-[4-(4-methyl-piperazin-1-ylmethyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidine;

{4-[4-(ethyl-methyl-amino)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone;

[4-(4-isopropylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phenyl]-(4-methyl-piperazin-1-yl)-methanone;

[4-(4-methylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phenyl]-(4-methyl-piperazin-1-yl)-methanone;

isopropyl-{6-[4-(4-methyl-piperazin-1-ylmethyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}-amine;

ethyl-methyl-{6-[4-(4-methyl-piperazin-1-ylmethyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}-amine;

{4-[4-(3-hydroxy-propylamino)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone;

methyl-{6-[4-(4-methyl-piperazin-1-ylmethyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}-amine;

(4-Methyl-piperazin-1-yl)-[4-(4-propylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phenyl]-methanone;

{6-[4-(4-Methyl-piperazin-1-ylmethyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}-propyl-amine;

methyl-{6-[4-(4-methyl-piperazin-1-ylmethyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}-propyl-amine;

[4-(4-Cyclopropylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phenyl]-(4-methyl-piperazin-1-yl)-methanone;

N-methyl-4-(4-methylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-benzamide;

{4-[4-(2-Dimethylamino-ethylamino)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone;

N,N-dimethyl-N'-{6-[4-(4-methyl-piperazin-1-ylmethyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}-ethane-1,2-diamine;

[6-(4-Imidazol-1-ylmethyl-phenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]-dimethyl-amine;

dimethyl-{6-[4-(1H-pyrrol-2-ylmethyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}-amine;

[6-(4-Butoxymethyl-phenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]-dimethyl-amine;

dimethyl-[6-(4-tetrazol-1-ylmethyl-phenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]-amine;

3-[4-(4-Dimethylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-benzylamino]-propan-1-ol;

[6-(4-[(2-Methoxy-ethyl)-methyl-amino]-methyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl]-dimethyl-amine;
3-{4-[4-(3-Morpholin-4-yl-propylamino)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-phenyl}-pentan-3-ol;
2-(4-{4-[Bis-(2-methoxy-ethyl)-amino]-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-phenyl}-propan-2-ol;
3-(4-{4-[Bis-(2-methoxy-ethyl)-amino]-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-phenyl}-pentan-3-ol;
3-{4-[4-(3-Pyrrol-1-yl-propylamino)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-phenyl}-pentan-3-ol;
2-[4-(4-Dimethylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phenyl]-propan-2-ol;
2-[4-(4-Methylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phenyl]-propan-2-ol;
or a pharmaceutically acceptable salt thereof.

6. A compound of formula I according to claim 1, 2, 3, 4 or 5 selected from the group consisting of

[4-(4-methylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phenyl]-morpholin-4-yl-methanone;
[4-(4-dimethylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phenyl]-morpholin-4-yl-methanone;
{4-[4-(ethyl-methyl-amino)-7H-pyrrolo[2,3-d]pyrimidin-6-yl]-phenyl}-(4-methyl-piperazin-1-yl)-methanone;
isopropyl-{6-[4-(4-methyl-piperazin-1-ylmethyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}-amine;
ethyl-methyl-{6-[4-(4-methyl-piperazin-1-ylmethyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}-amine;
methyl-{6-[4-(4-methyl-piperazin-1-ylmethyl)-phenyl]-7H-pyrrolo[2,3-d]pyrimidin-4-yl}-amine;
[6-(4-Imidazol-1-ylmethyl-phenyl)-7H-pyrrolo[2,3-d]pyrimidin-4-yl]-dimethyl-amine;
2-[4-(4-Dimethylamino-7H-pyrrolo[2,3-d]pyrimidin-6-yl)-phenyl]-propan-2-ol;
or a pharmaceutically acceptable salt thereof.

7. A compound of formula I, or a pharmaceutically acceptable salt thereof, according to any one of claims 1 to 6 for use in a method for the treatment of the human or animal body.

8. A pharmaceutical composition comprising a compound of formula I or a pharmaceutically acceptable salt thereof according to any one of claims 1 to 6, together with at least one pharmaceutically acceptable carrier.

9. a compound of formula I according to any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof for use as a pharmaceutical.

10. Use of a compound of formula I according to any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, for the preparation of a pharmaceutical composition for the treatment of a disease.

11. Use of a compound of formula I according to any one of claims 1 to 6, or a pharmaceutically acceptable salt thereof, for the preparation of a pharmaceutical composition for the treatment of a disease which responds to an inhibition of a protein tyrosine kinase.

12. A method of inhibiting Bcr-Abl in a subject in need of such treatment which method comprises administering to said subject an effective amount of an agent of the invention, or a method of treating any of the above mentioned conditions, particularly a method of treating a proliferative disease or condition, or alleviating one or more symptoms of any of the above mentioned conditions.

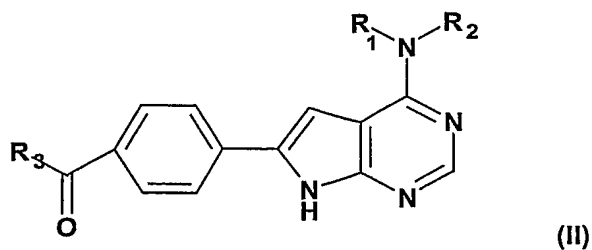
A compound according to claim 1 for use as a pharmaceutical, or for use in the prevention, amelioration or treatment of any disease or condition as described above.

A pharmaceutical composition comprising an agent of the invention in association with a pharmaceutically acceptable diluent or carrier, e.g., for use as an anti-proliferative agent or for use in the prevention, amelioration or treatment of any disease or condition as described above.

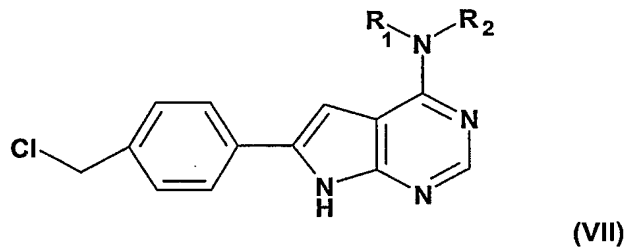
Use of a compound according to claim 1 in the manufacture of a medicament for use as an anti-proliferative agent or for use in the prevention, amelioration or treatment of any disease or condition as described above.

13. A process for the preparation of a compound of formula I according to claim 1 or of a salt thereof, wherein

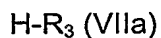
a) reduction of a compound of formula II



b) coupling a compound of formula 7

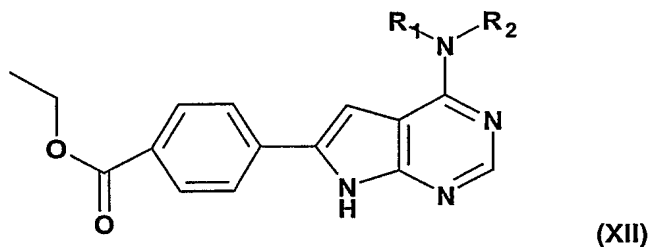


With a compound of formula VIIa,



wherein R_3 of formula VIIa is unsubstituted or substituted amino, heterocycle or heteroaryl.

c) for compounds wherein Y in formula 1 is of formula 2 as previously defined. Conversion of a compound of formula XII



with an organometallic compound of formula XIII



wherein Z is a halide and R_3 is a previously defined.

14. All novel compounds, methods, processes and uses substantially as hereinbefore described with particular reference to the examples.